REMARKS

Claims 31, 32, 56, 58, 62-66, 73, 75-80, and 82-108 are pending. Applicants have amended claims 56, 75, 83, 84, 95, and 108.

Claim Objections

The Office Action at pages 3-4 alleges that claims 106 and 107 are of improper dependent form for "failing to further limit the subject matter of a previous claim." The Office Action further states that "The recitation of 'further comprising selecting one or more members ...' in each of the claims does not further limit the subject matter of the claims from which they depend, but rather add an additional step" (*Id.*).

Applicants respectfully disagree because the additional step recited in claims 106 and 107 is an additional claim element that properly narrows the claims. To practice the method of claim 105, a library of compounds is screened for the ability of library members to interact with a transported polypeptide. A library can be screened without selection of any of its members. For example, some fee-for-service companies might screen libraries and report raw data to a client without selecting a member of the library. In contrast, to practice the method recited in claim 105, one or more members of the library that stimulate or inhibit (claim 106 or 107, respectively) must then be selected. This requires further action beyond screening a library for members that interact with a transporter polypeptide. Thus, Applicants submit that the requirement in claims 106 and 107 to perform an additional step beyond the steps recited in the method of claim 105 properly narrows the scope of these claims as compared to claim 105, and request that this objection be withdrawn.

35 U.S.C. § 112, 1st Paragraph, New Matter

The Office Action at page 4 has rejected claims 83-103 and 108, alleging that "the claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the art that the inventor(s), at the time the

application was filed, had possession of the claimed invention." The Office Action alleges that the terms "detecting the rate of aging of the cell" and "measuring the lifespan of the cell" are new matter.

Without conceding the point, Applicants have amended claims 83 and 84 to no longer include the term "detecting the rate of aging of the cell," thereby obviating this rejection. Applicants have also amended claim 108, although the rejection was moot with respect to this claim because the term at issue was not recited therein. Support for the term "assaying lifespan extension" recited in amended claims 83, 84, and 108 can be found in the specification, for example, at page 29:

> In another embodiment, an assay is a cell-based assay comprising contacting a cell expressing INDY with a test compound and determining the ability of the test compound to modulate (e.g. stimulate or inhibit) the activity of INDY ... Cell-based systems can be used to identify compounds that inhibit INDY ... After exposure, the cells are assayed, for example, for expression of the Indy gene or the INDY protein. Alternatively, the cells are assayed for phenotypes such as those resembling body weight disorders or lifespan extension. The cells may also be assayed for the inhibition of the transporter function of INDY. (emphasis added)

Applicants submit that this example clearly indicates that assaying lifespan extension of a cell was contemplated and described in the specification as filed.

35 U.S.C. § 101

The Office Action alleges at page 5 that claims 31, 32, 56, 58, 62-66, 73, 75-80, and 82-108 are not supported by a specific, substantial, and credible utility or a well-established utility. Applicants respectfully request that this rejection be withdrawn, because according to the standards set forth in the U.S. Patent and Trademark Office's Revised Interim Utility Guidelines Training Materials of 1999 ("Utility Guidelines"), the MPEP, and the courts, the application discloses an adequate utility.

The inquiry regarding utility is directed to the claimed subject matter, i.e., the methods recited in the claims. The methods recited in claims 31, 32, 56, 58, 62-66, 73,

and 82-108 have specific, substantial, and credible utility. The methods recited in these claims are drawn to assessing the inhibitory activity of a test compound on a transporter polypeptide, assessing the interaction of a test molecule with a transporter polypeptide, and assessing the ability of a test molecule to modulate expression of a transporter polypeptide.

As stated in MPEP § 2107.01(I):

> Some confusion can result when one attempts to label certain types of inventions as not being capable of having a specific and substantial utility based on the setting in which the invention is to be used. One example is inventions to be used in a research or laboratory setting. Many research tools such as gas chromatographs, screening assays, and nucleotide sequencing techniques have a clear, specific and unquestionable utility ... (emphasis added)

Also, the Court of Appeals for the Federal Circuit determined in *In re Brana* (51 F.3d 1560 (1995)) that "Usefulness in patent law, and in particular in the context of pharmaceutical inventions, necessarily includes the expectation of further research and development. The stage at which an invention in this field becomes useful is well before it is ready to be administered to humans" (*Id.* at 1568; emphasis added). Thus, Applicants submit that the claims satisfy the utility requirement standard set forth by the Utility Guidelines, the MPEP, and the courts.

Following the flowchart set forth on page 9 of the Utility Guidelines, the first inquiry is whether the applicants have made any assertion of utility. Indeed, Applicants have made such an assertion here. For example, pages 28-29 describe using the methods recited in these claims to identify molecules that modulate transporter polypeptide (e.g., INDY) function, and using such molecules to ameliorate body weight disorders or increase lifespan. Further, the molecules identified by the recited methods can be used to treat metabolic disorders, obesity, and aging symptoms, as described on page 23. These passages identify the asserted utility of the methods recited in claims 31, 32, 56, 58, 62-66, 73, and 82-108.

The second inquiry is whether the assertion identifies a specific utility. Applicants' asserted utility is specific. According to the Utility Guidelines, a utility is specific in the sense that it "contrasts with a *general* utility that would be applicable to the broad class of the invention" (page 5). The "broad class" of the invention here is screening methods. As stated above, the methods encompassed by the claims can be used to specifically identify molecules that inhibit, interact with, or modulate expression of transporter polypeptides such as INDY. This utility is specific, for example, to the transporter polypeptide sequences recited in the claims, SEQ ID NOs: 2, 3, 4, 5, and 6. Not any polypeptide could be used in practicing the claimed methods. Thus, the claims meet the "specific" criterion of the Utility Guidelines.

The third inquiry is whether the assertion identifies a substantial utility. According to the Utility Guidelines, a utility is substantial if it defines a "real world" use (page 6). The specific utility asserted by Applicants is substantial because it does define a real world use: The methods recited in the claims can be used to identify molecules that modulate transporter polypeptides.

Given the role of these transporter polypeptides in body weight disorders and longevity, the methods can be used to screen for substances useful in treating conditions such as metabolic disorders, obesity, and aging symptoms. As stated on page 6 of the Utility Guidelines, "both a therapeutic method of treating a known or newly discovered disease and an assay method for identifying compounds that themselves have a 'substantial utility' define a 'real world' context of use" (emphasis added). The methods recited in the claims provide an assay to identify molecules that have a substantial utility in modulating transporter polypeptides. The molecules have a "real world" utility. Thus, methods used to identify such molecules, e.g., the methods recited in claims 31, 32, 56, 58, 62-66, 73, and 82-108, also have a "real world" utility.

The final inquiry is whether this asserted, specific, and substantial utility is credible. The Utility Guidelines state on page 5 that "[a]n assertion is credible unless (A) the logic underlying the assertion is seriously flawed, or (B) the facts upon which the

assertion is based are inconsistent with the logic underlying the assertion." The Examiner has not provided any evidence that the logic of Applicants' assertion of utility is seriously flawed or that the assertion is inconsistent with the logic underlying it, and thus has not met the *prima facie* burden of showing a lack of utility. Further,

> Where the asserted specific and substantial utility is not credible, a *prima facie* showing of no specific and substantial credible utility must establish that it is more likely than not that a person skilled in the art would not consider credible any specific and substantial utility asserted by the applicant for the claimed invention. (MPEP § 2107.02 (IV)).

The Pajor et al. reference (*Annu. Rev. Physiol.* 61:663-682 (1999)) cited by the Office Action does not establish "that it is more likely than not that a person skilled in the art would not consider credible any specific and substantial utility asserted by the applicant for the claimed invention." Pajor et al. describes that three different types of sodium-coupled transporters exist: low-affinity, intermediate-affinity, and high-affinity transporters. The NaDC-1 family of transporters, which includes the transporter polypeptides recited in the methods of the claims, falls into the low-affinity type of transporters. This NaDC-1 family appears to be unique and "not related to any of the other transporter superfamilies" (Pajor et al. at 671). The Office Action states at page 7 that "The art teaches that sodium dicarboxylate cotransporters exhibit broad substrate specificities and carry a wide range of di- and tricarboxylic acids..." and "Pajor also discloses that different sodium-coupled dicarboxylate transporters differ in substrate affinity and substrate specificity, and that individual transporters exhibit functional differences between species." However, these assertions are of no consequence to the issue at hand. Diversity among transporters does not mean that the transporters here, members of the NaDC-1 family, do not function as the application states. Pajor et al. is devoid of a statement that "more likely than not" would lead a skilled person to doubt the credibility of any specific and substantial utility asserted by the Applicants.

The Office Action at page 8 alleges that the present situation is "directly analogous to that which was addressed in *Brenner v. Manson*." Applicants respectfully

disagree because the disclosure of the instant application differs substantially from that of the patent at issue in *Brenner v. Manson*, 383 U.S. 519 (1966). *Brenner* turned on the fact that the claimed process produced a compound that had no known function. The disclosure in *Brenner* did not provide a utility. The best evidence of utility that the respondent in *Brenner* proffered was a suggestion that related compounds, but not ones produced by the claimed process, inhibited tumors (383 U.S. at 531). In contrast, this is not a case where the transporter polypeptides recited in the methods of the claims have no known function. As described in the specification, the transporter polypeptides have well-characterized functions, as do the methods that utilize the polypeptides. For example, Example 4 describes the characterization of the INDY gene product, Example 6 describes the biological functions of INDY, including studies demonstrating that INDY is a transporter polypeptide and characterization of the effects of various transport inhibitors on INDY, Example 7 describes the effect of INDY on the fertility and physical activity of flies, and pages 24-25 describe the utility of the assay methods. Further, the test molecules identified in the screening methods have a utility: they inhibit the activity of, interact with, or modulate the expression of the transporter polypeptide. These disclosed utilities are more than adequate to satisfy the statutory threshold.

Finally, *Brenner* cannot stand for the sweeping proposition that all screening methods have inadequate utility. The defect in *Brenner* was that the application did not disclose a utility for the compound produced by the claimed process. In contrast, as described above, the transporter polypeptides and the molecules that modulate them have a utility. The oft-quoted language – that "a patent is not a hunting license" – means only that an applicant cannot seek patent protection without having enough information to disclose at least one utility for the invention. The present application discloses at least one utility for the invention.

Fujikawa v. Wattanasin, 93 F.3d 1559 (Fed. Cir. 1996), also compels the conclusion that the defect in *Brenner* was the complete absence of a disclosed utility.

This Federal Circuit decision, reached 30 years after *Brenner,* represents a modern understanding of *Brenner*. The Federal Circuit declared that:

> In the pharmaceutical arts, our court has long held that practical utility may be shown by adequate evidence of any pharmacological activity. Such activity constitutes a practical utility because it is inherently faster and easier to combat illnesses and alleviate symptoms when the medical profession is armed with an arsenal of chemicals having known pharmacological activities. Since it is crucial to provide researchers with an incentive to disclose pharmacological activities in as many compounds as possible, we conclude that adequate proof of any such activity constitutes a showing of practical utility. (93 F.3d at 1564; citations and internal quotations omitted; emphasis added)

Here, as was deemed sufficient in *Fujikawa*, the identified molecules have a pharmacological activity as they would modulate a transporter polypeptide, such as INDY.

The claimed methods themselves are also worthy additions to the arsenal available to the medical profession. As demonstrated in the attached press releases dated June 3, 2002 and November 16, 2004 (Exhibits A and B), Elixir Pharmaceuticals, Inc. has licensed the rights to study the INDY polypeptide and its human homolog, NaCT-1. The company believes that using these proteins will be useful, *inter alia*, in methods to identify new molecules for the treatment of diseases and disorders. If the claimed methods lacked utility, such technology would not be the subject of licenses.

The Office Action alleges at page 10 that "There is no evidence of record that would support a conclusion that compounds that bind to it [transporter polypeptide] or modulate the activity or expression of the proteins of the instant invention would be useful for treating hyperglycemia, diabetes, chronic obesity, metabolic disorders ..." Again, the Applicants point out that the *prima facie* burden is on the Office to establish that it is more likely than not that a person skilled in the art would not consider credible any specific and substantial utility asserted by the applicant for the claimed invention (MPEP § 2107.02(IV)). Second, the utility of the methods recited in these claims stems, in part, from the discovery by the Applicants that the *Drosophila* INDY protein is

involved in modulating the lifespan of flies. *Drosophila*, like *Saccharomyces cerevisiae*, *Saccharomyces pombe*, *Caenorhabditis elegans*, zebrafish, rats, and mice, are model organisms commonly used to study biological processes, such as those present in more complex organisms, e.g., humans. This is especially likely when the higher organism possesses a homolog of the protein or pathway present in the model organism. In the instant case, examples of human homologs of INDY are described on page 23. The results of studies in model organisms often correlate with and are translatable to higher species, such as humans, yet these models offer a system in which to manipulate and test processes, and elucidate biological mechanisms rather than studying processes in more complex organisms. For example, Fortini et al. (*J. Cell Biol.* 150:F23-F29 (2000); a copy of which is provided as Exhibit C) surveyed the presence of human disease genes in *Drosophila*. As described in page F26, "Categories [of human disease] with a high representation of homologues in *Drosophila* include the genes for ... metabolic disorders (14 of 17, 82%) ..." Fortini et al. concluded, "*Drosophila* appears to represent a particularly good model organism for the study of genes implicated in many cancers, neurological disease, malformation syndromes, metabolic disorders and some renal diseases ... Most promisingly, our search for fruit fly homologues of 287 known human disease genes leads us to conclude that as additional human disease genes are discovered, it is more likely than not that a counterpart will be found in the *Drosophila* genome" (*Id.* at F29; emphasis added). Applicants submit that a skilled practitioner would recognize the utility of a model organism and would consider results obtained in a model organism to be credible and to support the specific and substantial utility asserted by the Applicants, especially because human homologs of INDY exist.

Applicants respectfully request that this rejection for lack of utility, and the related lack of utility rejection under 35 U.S.C. § 112, 1st paragraph, of claims 31, 32, 56, 58, 62-66, 73, and 82-108 be withdrawn.

Claims 75-80 recite a method to assess the transport activity by a transporter polypeptide that comprises SEQ ID NO:2 and also have a specific, substantial, and

credible utility, as established by following the analysis set forth in the flowchart on page 9 of the Utility Guidelines, and according to the MPEP (see e.g., § 2107.01(I)) and the courts. First, Applicants have made an assertion of utility. For example, underexpression of the transporter gene or reduced activity of the transporter polypeptide can have deleterious consequences, such as metabolic imbalances. Practicing the methods recited in the claims allows a skilled practitioner to determine if transporter activity is decreased, and if yes, a subject with the decreased transporter activity can be treated. The methods allow for diagnosis of a condition characterized by decreased transporter activity (see, e.g., pages 36-37). Thus, Applicants have asserted a utility for the methods recited in claims 75-80.

The next inquiry is whether the assertion identifies a specific utility. Applicants' asserted utility is specific. The "broad class" of the invention here is a method of assessing protein function. As stated above, the methods encompassed by the claims can be used to specifically identify whether a transporter polypeptide that comprises SEQ ID NO:2 has decreased activity. This utility is specific to the transporter polypeptide sequence recited in the claims, i.e., SEQ ID NO:2. Further, not all methods can be used to identify molecules that modulate or interact with the encoded transporter polypeptide, because not all methods involve steps that allow identification of such decreased activity. The methods recited in these claims are specific, i.e., not general, and are not broadly applicable to the broad class of methods. Thus, the claims meet the "specific" criterion of the Utility Guidelines.

The next inquiry is whether the assertion identifies a substantial utility. According to the Utility Guidelines, a utility is substantial if it defines a "real world" use (page 6). The specific utility asserted by Applicants is substantial because it does define a real world use: The methods recited in the claims can be used to determine the transport activity of the transporter polypeptide. As an example, given the role of decreased transport by the transporter polypeptide in metabolic imbalances, the methods have a real world use of allowing diagnosis of such conditions. Once decreased transport activity is

identified, it can be treated, e.g., therapeutically. This defines a substantial, real world use.

The final inquiry is whether this asserted, specific, and substantial utility is credible. The Utility Guidelines state on page 5 that "[a]n assertion is credible unless (A) the logic underlying the assertion is seriously flawed, or (B) the facts upon which the assertion is based are inconsistent with the logic underlying the assertion." The Examiner has not provided any evidence that the logic of Applicants' assertion of utility is seriously flawed or that the assertion is inconsistent with the logic underlying it, and thus has not met the prima facie burden of showing a lack of utility (MPEP § 2107.02 (IV)). Thus, Applicants respectfully request that this rejection for lack of utility, and the related lack of utility rejection under 35 U.S.C. § 112, 1st paragraph, of claims 75-80 be withdrawn.

35 U.S.C. § 112, Second Paragraph

The Office Action alleges at page 11 that claims 31, 32, 82-103, and 108 are indefinite "because it is unclear if the newly added limitation 'has been expressed by a cell' refers to a polypeptide that is present in the cell or a polypeptide that has simply been expressed by a cell and, for example, now isolated and purified." Applicants submit that these claims are clear: the polypeptide was expressed by a cell. The polypeptide can be present in the cell or it can be isolated and purified from such a cell. The claims include both of these, and cell-based and cell-free assays are both described in the application, e.g., at page 29.

The Office Action alleges at page 11 that claims 56, 66, and 104 are indefinite "because claim 56 does not have a step that clearly relates back to the preamble." Without conceding the point, Applicants have amended claim 56 to include a step that clearly relates back to the preamble.

The Office Action alleges at page 11 that claims 75-80 are indefinite for omitting essential steps, "such omission amounting to a gap between the steps" and that "'assessing transport' does not set forth any steps involved in the method/process,

therefore it is unclear what method/process is encompassed by the claim." Without conceding the point, Applicants have amended claim 75 to recite the step of "detecting the substrate to determine transport of the substrate into the cell."

The Office Action alleges at page 11 that claims 83-103 and 108 are indefinite "because the claims do not have a step that clearly relates back to the preamble." Without conceding the point, Applicants have amended claims 83, 84, and 108 to include a step that clearly relates back to the preamble.

The Office Action alleges at page 11 that claims 83-103 and 108 are indefinite "for reciting the phrase 'contacting the test molecule to a cell' in the penultimate line of the claim. It is unclear whether 'a cell' refers to the same cell mentioned in the first part of the claim or if it refers to a different cell." Without conceding the point, Applicants have amended claims 83, 84, and 108 to indicate that the methods recited in these claims involve a two-step screening process: the test molecule is contacted with the transporter polypeptide and it is also contacted with a cell in a separate step.

The Office Action alleges at page 11 that claims 83-103 and 108 are indefinite for the reasons set forth at page 3 of the Office Action mailed December 3, 2004, namely, for failing to define "what is being measured by measuring the rate of aging." Without conceding the point, Applicants have amended claims 83, 84 and 108 to indicate that lifespan extension is assayed.

CONCLUSION

The Applicants respectfully submit that all claims are in condition for allowance, which action is expeditiously requested. The Applicants do not concede any positions of the Examiner that are not expressly addressed above. All amendments and cancellations are made without prejudice and disclaimer and may be made for reasons not explicitly stated or for reasons in addition to ones stated.

Attorney's Docket No.: 13407-012001 / 00-066

Enclosed is a $510 check for the Petition for Extension of Time fee. Please apply any other charges or credits to deposit account 06-1050.

Respectfully submitted,

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